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REGULAR ARTICLE

Gold-catalyzed formation of substituted aminobenzophenone derivatives *via* intramolecular *6-endo-dig* cyclization

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Dedicated to Doma Gowthami on the occasion of her birthday.

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Abstract. An efficient and straightforward synthetic method to access substituted aminobenzophenones has been developed. This transformation was catalyzed by gold and a new C—C bond was formed through intramolecular *6-endo-dig* cyclization. The substituted aminobenzophenones were obtained in good to excellent yields.

Keywords. Aminobenzophenones; Cascade reaction; Gold catalysis; *6-endo-dig* cyclization.

1. Introduction

Substituted aminobenzophenones are privileged structural motifs that are present in many natural products and pharmaceuticals (Figure 1).[1] In particular, they exhibit a broad spectrum of biological activity such as antitumor,[2] antiproliferative,[3] antimitotic,[4] agents, and skeletal muscle relaxant.[5] Some of these derivatives are useful in the preparation of functional materials.[6] They have also been found as important synthons for the synthesis of biologically active molecules.[7] In the view of their applications in medicinal chemistry and material science, the development of improved methods for the preparation of substituted aminobenzophenones received considerable attention in modern organic chemistry.[8] Therefore, various synthetic strategies have been reported in the literature for the synthesis of substituted aminobenzophenones.[9] However, all of these substrates are limited to specific substitutions and long reaction times.

Homogenous gold catalysis has become one of the emerging tools in organic synthesis.[10] As a result, gold-catalyzed cyclizations of conjugated dienynes has been extensively studied for the construction of highly functionalized scaffolds in recent years.[11] Very few research groups have reported gold-catalyzed-cyclization reactions of enynes.[12] In 2008, Barluenga and Aguilar *et al.,* developed a Gold-Catalyzed Intermolecular Hetero-Dehydro-Diels-Alder Cycloaddition of Captodative Dienynes with Nitriles (Scheme 1a).[13] Later, Aguilar *et al.,* reported a gold-catalyzed 2,7-cycloaromatization reaction of captodative dienyne carboxylic acids (Scheme 1b).[14] Roberto Sanz *et al.,* developed a gold-catalyzed unprecedented tandem cyclization-migration sequence of 1,1-disubstituted-1,3-hexadien-5-ynes (Scheme 1c).[15] Very recently, Weiwei Zi *et al.,* reported Rh(I)-catalyzed oxidative cycloaromatization reaction for *de novo* synthesis of polysubstituted naphthols and phenols.[16] On the other hand, Ru, Fe and Pt catalysts promoted cyclization reactions of conjugated dienynes reported in the literature.[17] Inspired by these limited approaches, and our ongoing investigations on gold-catalyzed organic

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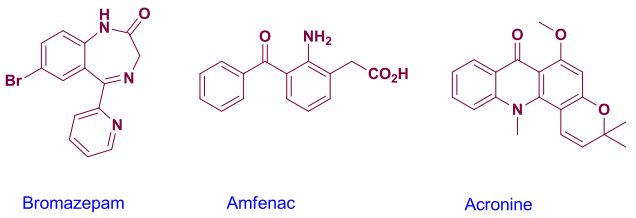
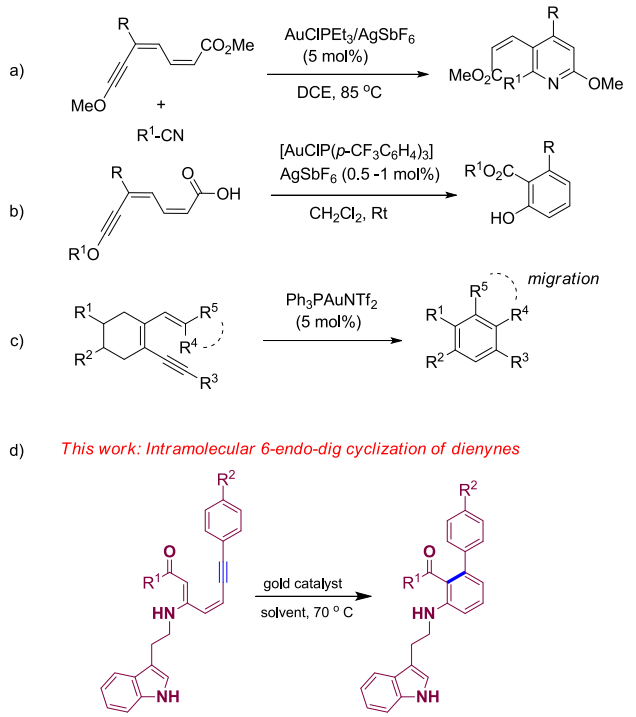


Figure 1. Biologically important aminobenzophenones derivatives.



Scheme 1. Different approaches for cyclization reactions of dienynes and present work.

transformations,[18] we envisioned that highly functionalized aminobenzophenone derivatives could be easily obtained by utilizing 7-oxo-1,7-diarylhepta-1,5-diyn-3-yl-benzoates in the presence of gold catalyst through Intramolecular *6-endo-dig* cyclization (Scheme 1d). Starting materials in turn synthesized by well-known reported procedures.[19]

2. Experimental

2.1 *General information*

All reactions were carried out in oven-dried reaction flasks under a nitrogen atmosphere and dry solvents and reagents were transferred by oven-dried syringes to ambient temperature. TLC was performed on Merck silica gel aluminium sheets and solvents were removed under reduced pressure. Columns were packed as a slurry of silica gel in hexane and ethyl acetate solvent mixture. The elution was assisted by applying pressure with an air pump. ^{13}C NMR spectra were recorded on 100 MHz spectrometers. ^{1}HNMR spectra were recorded on 400 and 500 MHz spectrometers in appropriate solvents using TMS as an internal standard. The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet. All reactions were performed under a nitrogen atmosphere with freshly distilled and dry solvents. All solvents were distilled using standard procedures. Unless otherwise noted, reagents were obtained from Aldrich, Alfa Aesar, and TCI used without further purification. Syntheses of substituted aminobenzophenones (**2a**-**n**) were prepared by following reported procedures.

2.2 *Representative experimental procedure for preparation substituted aminobenzophenone 2a*

To a 10 mL round-bottomed flask equipped with magnetic stir bar compound 3-(alkylamino)-1,7-diphenylhepta-2,4-dien-6-yn-1-one **1a** (0.13 g, 0.3 mmol, 1 equiv.) was taken and dissolved in MeOH (3 mL). To this reaction mixture IPrAuCl (0.018 g, 10 mol%)/$AgNTf_2$ (0.017 g, 15 mol%) was added and stirred at 70 °C temperature for 4 h under nitrogen atmosphere. The progress of the reaction was monitored using TLC. After completion of the reaction, the reaction mixture was filtered through a celite plug and washed the celite plug with Ethyl acetate. The Ethyl acetate layer was concentrated under reduced pressure to get crude residue which was purified by column chromatography through silica gel using hexane and ethyl acetate as eluent (10:1.5) to give pure **2a** in (0.112 g, 90%). A similar procedure was followed for the synthesis of all substituted aminobenzophenones derivatives (**2b-2n**).

2a: Brown viscous liquid: Yield: 90%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.59 (t, J = 6.1 Hz, 1H), 7.43–7.37 (m, 3H), 7.36–7.32 (m, 1H), 7.24–7.17 (m, 2H), 7.17–7.12 (m, 2H), 7.12–6.99 (m, 7H), 6.82 (d, J = 7.8 Hz, 1H), 6.71 (dd, J = 7.5, 0.8 Hz, 1H), 5.53 (d, J = 44.9 Hz, 1H), 3.48 (t, J = 7.0 Hz, 2H), 3.07 (t, J = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.5, 147.4, 142.9, 141.4, 139.4, 136.2, 132.0, 131.4, 129.3, 129.2, 127.8, 127.6, 127.1, 126.9, 122.1, 122.0, 121.9, 119.2, 118.6, 117.8, 113.1, 111.1, 110.2, 43.7, 24.9.

2b: Brown viscous liquid: 83%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (d, J = 8.5 Hz, 1H), 7.94 (s, 1H), 7.66–7.58 (m, 3H), 7.45 (ddd, J = 8.4, 6.9, 1.3 Hz, 1H), 7.42–7.35 (m, 2H), 7.32 (d, J = 8.1 Hz, 1H), 7.21–7.03 (m, 5H), 6.94 (d, J = 7.6 Hz, 2H), 6.87 (d, J = 8.5 Hz, 1H), 6.71 (t, J = 7.6 Hz, 2H), 6.60 (t, J = 7.9 Hz, 2H), 3.57 (t, J = 7.1 Hz, 2H), 3.14 (t, J = 7.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.6, 148.9, 145.0, 141.8, 138.8, 136.3, 133.2, 132.2, 131.5, 130.4, 128.8, 128.7, 127.7, 127.3, 127.2, 126.8, 125.9, 125.8, 123.7, 122.6, 122.1, 121.9, 119.2, 118.6, 117.9, 113.1, 111.1, 110.2, 43.7, 25.1.

2c: Brown viscous liquid: Yield: 82%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.80 (s, 1H), 7.70 (dd, *J* = 10.3, 6.2 Hz, 2H), 7.63–7.55 (m, 3H), 7.51–7.47 (m, 1H), 7.45–7.39 (m, 2H), 7.28–7.25 (m, 2H), 7.18–7.12 (m, 3H), 7.10–7.04 (m, 1H), 6.99–6.94 (m, 3H), 6.88 (ddd, *J* = 15.3, 7.9, 4.6 Hz, 2H), 6.76 (dd, *J* = 7.5, 0.8 Hz, 1H), 5.42 (d, *J* = 7.5 Hz, 1H), 3.56–3.44 (m, 2H), 3.06 (t, *J* = 6.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 200.2, 147.4, 142.9, 141.5, 136.5, 136.2, 134.9, 132.0, 131.3, 131.3, 129.3, 128.9, 128.0, 127.9, 127.8, 127.7, 127.6, 127.4, 127.1, 126.8, 126.2, 124.7, 122.3, 122.0, 119.2, 118.5, 118.0, 113.0, 111.1, 110.3, 43.7, 24.9.

2d: Brown viscous liquid: Yield: 82%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.41–7.36 (m, 2H), 7.32–7.25 (m, 2H), 7.24–7.19 (m, 1H), 7.15–7.07 (m, 3H), 7.02 (dd, *J* = 8.2, 6.6 Hz, 3H), 6.97 (ddd, *J* = 7.3, 3.7, 1.3 Hz, 1H), 6.92 (d, *J* = 2.2 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 6.66 (dd, *J* = 7.5, 0.8 Hz, 1H), 6.55–6.50 (m, 2H), 5.05 (s, 1H), 3.67 (s, 3H), 3.43–3.30 (m, 2H), 2.98 ppm (t, *J* = 6.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 198.8, 162.918, 146.8, 142.1, 141.3, 136.2, 131.8, 131.7, 130.8,129.0, 127.8, 127.2, 126.9, 122.9, 122.0, 121.9, 119.2, 118.6, 117.9, 113.0, 113.0, 111.1, 110.1, 55.2, 43.8, 24.9.

2e: Brown viscous liquid: Yield: 75%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.39–7.32 (m, 4H), 7.18 (tt, *J* = 6.1, 3.1 Hz, 1H), 7.15–7.12 (m, 2H), 7.11–7.08 (m, 3H), 7.06–7.01 (m, 3H), 7.00–6.95 (m, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.71 (d, *J* = 7.5 Hz, 1H), 5.52 (s, 1H), 3.47 (t, *J* = 7.1 Hz, 2H), 3.06 (t, *J* = 7.0 Hz, 2H), 1.20 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 200.2, 155.5, 147.2, 142.9, 141.5, 136.6, 136.3, 131.1, 129.2, 127.7, 127.2, 126.7, 124.5, 122.4, 122.1, 122.0, 119.3, 118.6, 117.8, 113.2, 111.1, 110.2, 43.8, 34.8, 30.9, 25.0.

2f: Brick viscous liquid: Yield: 70%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.44–7.37 (m, 3H), 7.36–7.30 (m, 1H), 7.20–7.00 (m, 8H), 6.82 (d, *J* = 8.3 Hz, 1H), 6.77–6.68 (m, 3H), 5.56 (s, 1H), 3.47 (t, *J* = 7.0 Hz, 2H), 3.07 (t, *J* = 7.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 198.9, 166.1, 163.5, 147.4, 142.8, 141.3, 136.3, 135.6, 131.8, 131.7, 131.5, 129.1, 127.9, 127.2, 127.1, 122.0, 121.7, 119.3, 118.6, 117.9, 114.8, 114.6, 113.0, 111.1, 110.3, 43.7, 24.9.

2g: Brown viscous liquid: 72%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.44– 7.36 (m, 3H), 7.31 (dd, *J* = 18.8, 8.2 Hz, 3H), 7.21–7.15 (m, 1H), 7.12–6.97 (m, 7H), 6.87–6.81 (m, 1H), 6.70 (dd, *J* = 7.5, 0.8 Hz, 1H), 6.00 (s, 1H), 3.51 (t, *J* = 6.9 Hz, 2H), 3.11 (t, *J* = 6.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 199.4, 148.1, 143.6, 143.0, 141.3, 136.3, 132.2, 129.3, 129.1, 128.0, 127.2, 127.2, 124.4, 122.1, 122.0, 120.7, 119.3, 118.6, 117.8, 113.0, 111.2, 110.5, 43.6, 25.0.

2h: Black viscous liquid: 78%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.36 (dd, *J* = 7.6, 6.4 Hz, 3H), 7.34–7.26 (m, 4H), 7.22–7.17 (m, 1H), 7.15–7.12 (m, 2H), 6.74 (d, *J* = 8.3 Hz, 1H), 6.65 (d, *J* = 7.4 Hz, 1H), 6.32 (d, *J* = 46.6 Hz, 1H), 3.47 (t, *J* = 7.0 Hz, 2H), 3.17–3.07 (m, 2H), 2.82 (p, *J* = 8.3 Hz, 1H), 1.92 (ddd, *J* = 11.5, 8.8, 2.1 Hz, 2H), 1.64–1.52 (m, 2H), 1.46–1.37 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 211.0, 146.7, 142.2, 142.0, 136.3, 131.3, 128.9, 128.5, 127.5, 127.2, 123.1, 122.1, 122.0, 119.3, 118.6, 118.0, 113.2, 111.1, 110.4, 47.0, 43.7, 25.6, 25.0, 17.2.

2i: Brown viscous liquid: 73%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (400 MHz, $CDCl_3$) : *δ* 7.94 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.44–7.39 (m, 2H), 7.38–7.31 (m, 2H), 7.27–7.23 (m, 2H), 7.20–7.15 (m, 1H), 7.12–7.06 (m, 3H), 7.05–6.99 (m, 3H), 6.88-6.84 (m, 2H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.70 (d, *J* = 7.4 Hz, 1H), 5.52 (s, 1H), 3.47 (t, *J* = 6.9 Hz, 2H), 3.06 (t, *J* = 6.9 Hz, 2H), 2.15 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) *δ* 200.6, 147.2, 142.8, 139.3, 138.5, 136.6, 136.3, 131.9, 131.3, 129.2, 129.1, 128.5, 127.6, 127.2, 122.2, 122.1, 122.0, 119.2, 118.6, 117.8, 113.1, 111.1, 110.0, 43.7, 25.0, 20.9.

2j: Brown viscous liquid: Yield: 71%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.43–7.39 (m, 2H), 7.39–7.30 (m, 2H), 7.29-7.27 (m, 2H), 7.21–7.15 (m, 1H), 7.12–7.07 (m, 3H), 7.06 - 6.99 (m, 3H), 6.88– 6.84 (m, 2H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.70 (d, *J* = 7.4 Hz, 1H), 5.51 (s, 1H), 3.47 (t, *J* = 6.9 Hz, 2H), 3.06 (t, *J* = 6.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 200.2, 147.1, 142.7, 138.5, 136.5, 136.3, 136.2, 135.0, 132.1, 131.3, 131.2, 129.4, 128.8, 128.6, 127.9, 127.6, 127.4, 127.1, 126.1, 124.8, 122.5, 122.0, 121.9, 119.2, 118.5, 118.0, 113.0, 111.1, 110.1, 43.7, 24.9, 20.8.

2k: Brown viscous liquid: Yield: 68%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.46–7.39 (m, 2H), 7.39–7.32 (m, 2H), 7.21–7.16 (m, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 7.9 Hz, 3H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.82–6.68 (m, 4H), 5.46 (s, 1H), 3.47 (t, *J* = 6.9 Hz, 2H), 3.07 (t, *J* = 7.0 Hz, 2H), 2.22–2.12 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 198.9, 165.9, 163.8, 147.2, 142.7, 138.4, 136.8, 136.3, 135.6, 131.8, 131.7, 131.4, 129.0, 128.6, 122.0, 119.3, 118.6, 117.9, 114.7, 114.6, 113.1, 111.1, 110.1, 43.7, 24.9, 20.9.

2l: Brown viscous liquid: 72%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.61–7.57 (m, 1H), 7.39 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.37–7.32 (m, 2H), 7.22–7.15 (m, 3H), 7.12–7.05 (m, 2H), 7.02 (d, *J* = 2.3 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 2H), 6.75 (ddd, *J* = 10.2, 7.0, 6.2 Hz, 3H), 5.21 (s, 1H), 3.46 (t, *J* = 10.2 Hz, 2H), 3.14– 2.96 (m, 2H), 2.21 (s, 3H). ^{13}C NMR (100 MHz,

$CDCl_3$): δ 191.9, 146.7,145.6, 141.8, 138.5, 136.7, 136.3, 134.8, 133.8, 131.2, 128.9, 128.8, 127.3, 127.2, 122.6, 122.0, 122.0, 119.3, 118.6, 118.1, 113.1, 111.1, 110.0, 43.8, 24.9, 21.0.

2m: Brown viscous liquid: Yield: 73%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.47–7.43 (m, 2H), 7.38–7.30 (m, 2H), 7.21–7.06 (m, 4H), 6.98 (d, *J* = 2.0 Hz, 1H), 6.78 (ddd, *J* = 9.7, 5.9, 2.6 Hz, 3H), 6.68 (dd, *J* = 7.5, 0.8 Hz, 1H), 6.64–6.58 (m, 2H), 5.13 (s, 1H), 3.76 (s, 3H), 3.44 (t, *J* = 7.0 Hz, 2H), 3.04 (t, *J* = 6.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.6, 163.0, 146.8, 140.9, 137.4, 136.3, 131.7, 131.5, 130.9, 130.6, 130.5, 127.2, 122.9, 122.0, 119.2, 118.6, 117.8, 114.9, 114.7, 113.2, 113.1, 111.1, 110.2, 55.3, 43.8, 24.9.

2n: Brown viscous liquid: Yield: 73%; R_f: 0.5; Hexane-Ethyl acetate mixture (10:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.60–7.56 (m, 1H), 7.44 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.39–7.30 (m, 2H), 7.27–7.24 (m, 3H), 7.19–7.15 (m, 1H), 7.10–7.06 (m, 1H), 7.04 (d, *J* = 2.6 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.86–6.80 (m, 2H), 6.75 (dd, *J* = 7.0, 6.2 Hz, 1H), 6.70–6.66 (m, 1H), 6.64–6.58 (m, 1H), 5.24 (s, 1H), 3.45 (t, *J* = 7.8 Hz, 2H), 3.05 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) : 191.7, 162.9, 160.9, 146.8, 145.4, 140.7, 137.5, 136.3, 134.8, 134.1, 131.3, 130.5, 130.5, 127.4, 127.1, 124.2, 122.6, 122.1, 122.0, 119.3, 118.6, 117.9, 115.1, 114.9, 113.0, 111.1, 110.3, 43.7, 24.9.

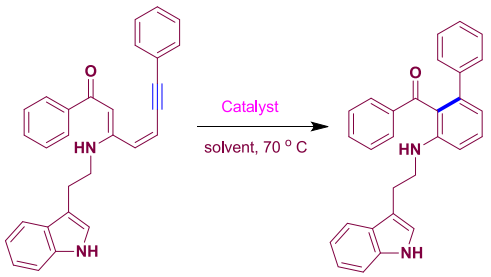
3. Results and Discussion

The initial experiments were carried out with 3-(alkylamino)-1,7-diphenylhepta-2,4-dien-6-yn-1-one (**1a**) to allow the optimization in several parameters as shown in Table 1. In our first attempt, the cyclized product **2a** was observed in 52% yield in the presence of AuCl (10 mol %) in MeOH (Entry 1, Table 1). The same reaction was carried out without utilizing catalysts in MeOH (Entry 2, Table 1). In this case, the reaction did not proceed, and the starting material remained intact. Encouraged by this result, we decided to screen this organic transformation with different catalysts and catalyst combinations. We tested the reaction of **1a** in the presence of $AuCl_3$ (10 mol%) gave a complex mixture of products (Entry 3, Table 1). When the reaction of substrate **1a** was conducted in the presence of $Au(PPh_3)][NTf_2]$ and [Au(JohnPhos)(MeCN)][SbF_6] catalysts, we have observed product **2a** in 48% and 44% yields (Entry 4 and 5, Table 1). We also conducted this reaction with different catalysts such as AgOTf, $Zn(OTf)_2$, CuBr, $AgNTf_2$, $AgNO_3$, and $AgSbF_6$. In all these cases, the reaction did not proceed (Entries 6–11, Table 1). The reaction of substrate **1a** in the presence of $In(OTf)_2$ produced the poor yields of product **2a** (Entry 12, Table 1). Gratifyingly, when the reaction was conducted in the presence of 10 mol% of IPrAuCl and 15 mol% of $AgNTf_2$ in MeOH gave the desired product **2a** in 90 % yield (Entry 13, Table 1). Next, we investigated the effect of the solvent on this organic transformation (Entries 14–19, Table 1). None of these gave any improvement on the yields of the product **2a**. We also performed experiments to check the catalyst loading effect on the rate of the reaction, when the was reaction conducted by utilizing 5 mol% of IPrAuCl and 15 mol% of $AgNTf_2$ in MeOH, a moderate yield of product **2a** was obtained (Entry 20, Table 1). The above results revealed that 10 mol% of IPrAuCl and 15 mol% of $AgNTf_2$ in MeOH at 70 °C are the best optimal conditions for the formation of product **2a** (Entry, 11, Table 1).

To evaluate the substrate scope for this reaction various substituted 3-(alkylamino)-1,7-diphenylhepta-2,4-dien-6-yn-1-ones were tested under the optimized reaction conditions. The results were shown in Table 2. The substrate **1b** (R^1 = 1-napthyl, R^2 = Ph) treated in the presence of 10 mol% of IPrAuCl and 15 mol% of $AgNTf_2$ afforded the desired product **2b** in 83% yield (Entry 2, Table 2). When the reaction tested with the substrate **1c** (R^1 = 2-napthyl, R^2 = Ph) obtained 82% yield of the desired product **2c**. Substrates containing electron-donating groups at the R^1 position such as **1d** (R^1 = 4-$OMeC_6H_4$, R^2 = Ph) and **1e** (R^1 = 4-*t*Bu-C_6H_4, R^2 = Ph) gave the corresponding products **2d** and **2e** in 80% and 75% yields respectively (Entry 4 and 5, Table 2). Electron-withdrawing substituted substrates such as **1f** (R^1 = 4-FC_6H_4, R^2 = Ph) and **1g** (R^1 = 4-$CF_3C_6H_4$, R^2 = Ph) was also well-tolerated and produced the desired products **2f** and **2g** in good yields (Entry 6 and 7, Table 2). It is noteworthy that the substrate **1h** (R^1 = cyc-FC_4H_7, R^2 = Ph) having cyclic substitution also provided the corresponding product **2h** in a 78% yield (Entry 8, Table 2).

We also tested the substrates, which are bearing electron donating groups such as **1i** (R^1 = Ph, R^2 = 4-MePh), **1j** (R^1 = 2-napthyl, R^2 = 4-MePh), **1k** (R^1 = 4-FPh, R^2 = 4-MePh) and **1l** (R^1 = 2-thiophene, R^2 = 4-MePh) under optimized conditions. In all the cases the desired products **2i-l** obtained in 73%, 71%, 68% and 72% yields, respectively (Entry 9-12, Table 2).

Table 1. Optimization of the reactions conditions.



1a **2a**

Entry	Catalyst (mol %)[a]	Solvent	Time (h)	Yield (%)[b]
1	AuCl (10)	MeOH	4	52
2	No catalyst	MeOH	4	n.r.[c]
3	$AuCl_3$ (10)	MeOH	1	c.m.[d]
4	$[Au(PPh_3)][NTf_2]$ (10)	MeOH	24	48
5	[Au(JohnPhos)(MeCN)] $[SbF_6]$ (10)	MeOH	12	44
6	AgOTf (10)	MeOH	6	n.r.[c]
7	$Zn(OTf)_2$ (10)	MeOH	12	n.r.[c]
8	CuBr (10)	MeOH	12	n.r.[c]
9	$AgNTf_2$ (15)	MeOH	12	n.r.[c]
10	$AgNO_3$ (10)	MeOH	7	n.r.[c]
11	$AgSbF_6$ (10)	MeOH	8	n.r.[c]
12	$In(OTf)_3$ (10)	MeOH	8	16
13	**IPrAuCl (10)/$AgNTf_2$ (15)**	**MeOH**	**3**	**90**
14	IPrAuCl (10)/$AgNTf_2$ (15)	DCM	18	62
15	IPrAuCl (10)/$AgNTf_2$ (15)	DCE	18	58
16	IPrAuCl (10)/$AgNTf_2$ (15)	$CHCl_3$	24	56
17	IPrAuCl (10)/$AgNTf_2$ (15)	CH_3CN	16	32
18	IPrAuCl (10)/$AgNTf_2$ (15)	DMF	36	45
19	IPrAuCl (10)/$AgNTf_2$ (15)	THF	36	39
20	IPrAuCl (5)/$AgNTf_2$ (15)	MeOH	5	59

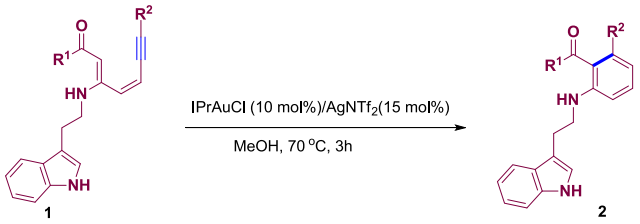
[a] Reactions conditions: reactions were conducted at nitrogen atmosphere with 1a (0.3 mmol) and the solvent (3 mL) at 70 °C; [b] yield for isolated products; [c] n.r. = no reaction; [d] c.m. = complex mixture.

Electron withdrawing substitution at the R^2 position for substrates like **1m** (R^1 = 4-OMePh, R^2 = 4-FPh) gave 73% yield of the corresponding product **2m** (Entry 13, Table 2). Significantly, heterocyclic substitution at R^1 position **1n** (R^1 = thiophene, R^2 = 4-F-Ph) also gave the desired product **2n** in 78% yield (Entry 14, Table 2).

Based on the above experimental result and previous reports,[20] a plausible mechanism could be proposed for this organic transformation (Scheme 2). In the presence of the gold catalyst, substrate **1a** would give intermediate **A**. This intermediate **A** would further undergo 6-*endo-dig* cyclization to give intermediate **B**, and would finally afford substituted aminobenzophenone **2a** *via* protodeauration.

In conclusion, we have developed a simple and new synthetic method to access substituted biphenyl derivatives. This reaction proceeds through intramolecular *6-endo-dig* cyclization followed by protodeauration in the presence of a gold catalyst. This strategy provides substituted aminobenzophenones in good to excellent yields with high functional group tolerance. It is expected that these derivatives are an important class of molecules, widely present in many pharmaceuticals. In the future, the biological significance of the synthesized derivatives was studied.

Table 2. Substrate scope of Aminobenzophenones.



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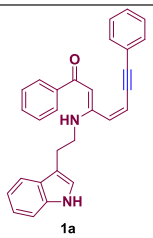
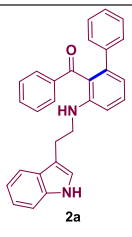
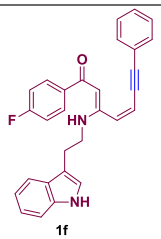
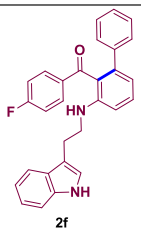
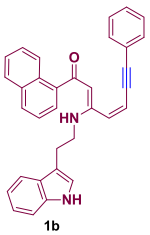
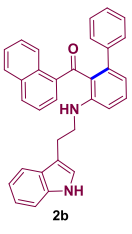
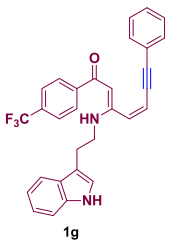
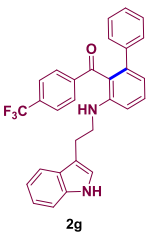
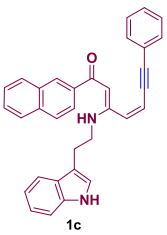
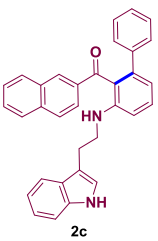
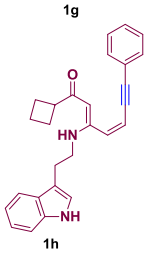
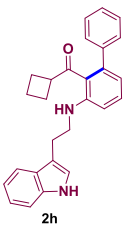
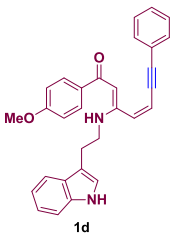
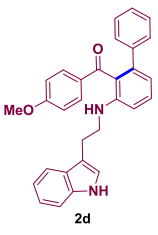
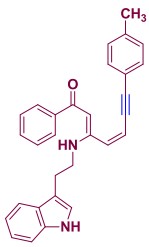
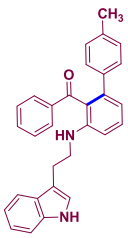
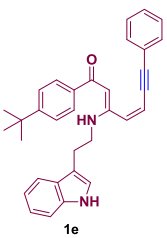
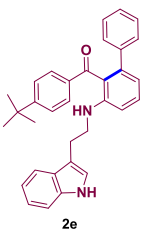
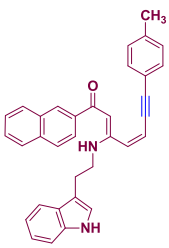
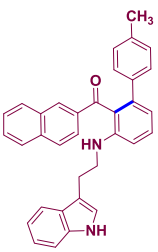
1	 1a	 2a	90	6	 1f	 2f	70
2	 1b	 2b	83	7	 1g	 2g	72
3	 1c	 2c	82	8	 1h	 2h	78
4	 1d	 2d	82	9	 1i	 2i	73
5	 1e	 2e	75	10	 1j	 2j	71

Table 2. continued

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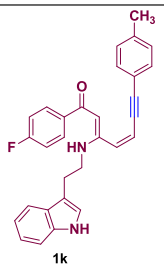
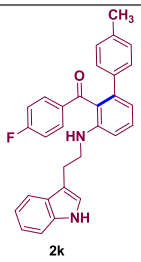
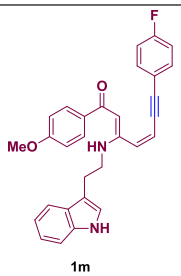
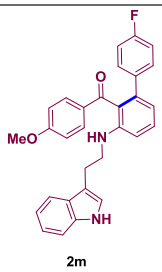
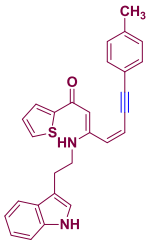
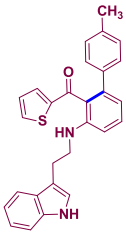
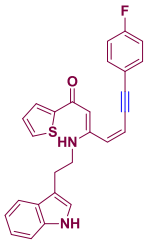
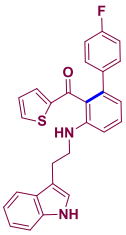
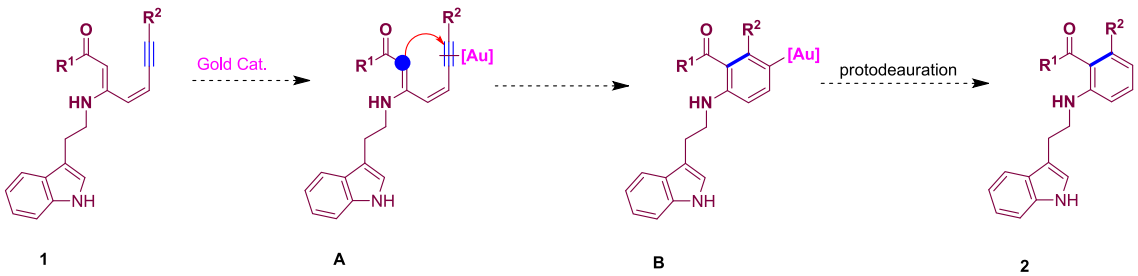
11	 1k	 2k	68	13	 1m	 2m	73
12	 1l	 2l	72	14	 1n	 2n	73

[a] Reaction conditions: All of the reactions were performed under a nitrogen atmosphere with compound 1a-1n (0.3 mmol), IPrAuCl (10 mol %)/$AgNTf_2$ (15 mol %) and MeOH (3 mL) at 70 °C. [b] yield of the isolated product.



Scheme 2. A plausible reaction mechanism.

Supplementary Information (SI)

^{1}H and ^{13}C NMR spectra of isolated compounds and are provided in the supporting information. Supplementary information is available at www.ias.ac.in/chemsci.

Acknowledgements

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